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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/908,950	GETTS ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on June 9, 2006 has been entered.

Status of the Application

2. Claims 1-56 are currently pending. Claims 1-56 are considered for examination in this office action. All amendments and arguments have been thoroughly reviewed and deemed persuasive in view of amendment. The instant amendment introduces new limitations in step (a) (ii) in claim 1, 19 and claim 52, that is, 'multiple first arms and multiple second arms' which are not present in the previously examined claims, thus the amendment introduced new limitations as shown above and changed the scope of the independent claims to overcome the rejection under 102(b). Accordingly the previous rejections are withdrawn and the following new combination of rejections has been applied to reject newly presented claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. This action is made Final, necessitated by Amendment.

New Grounds of Rejections necessitated by amendment

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779).

Dellinger et al. teach a method of claims 1, 47, for determining the presence or absence of a specific nucleic acid sequence in an RNA reagent of a target sample, said method comprises (a) incubating a mixture comprising (i) a first component including an RNA reagent (mRNA) extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7); (ii) a second component comprising a capture reagent (reporter probe) comprising a label capable of emitting a detectable signal and a nucleotide sequence complementary to the capture sequence of the RNA reagent of the first component (see col. 4, line 44-45, col. 5, line 7-12, line 23-46), at a first temperature to induce hybridization and thereby to form a pre-hybridized RNA-capture reagent complex (reporter-analyte complex (see col. 5, line 34-46); (b) contacting pre-hybridized RNA-Capture complex with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 4, line 44-46); (d) incubating said mixture at a second temperature to induce hybridization between pre-hybridized

RNA-capture reagent complex and the probe on the array, and detecting the he hybridization pattern (col. 4, line 46-49, col. 7, line 27-58).

With regard to claim 2, 20, 49, Dellinger et al. teach that the capture reagent includes carbohydrates, proteins and nucleic acids (see col. 3, line 32-37, col. 8, line 60-62);

Dellinger et al. teach a method of claims 3, 44, for determining the presence or absence of a specific nucleic acid sequence in an RNA reagent of a target sample, said method comprises (a) incubating a mixture comprising (i) a first component including an RNA reagent (mRNA) extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7); (ii) a second component comprising a capture reagent (reporter probe) comprising a label capable of emitting a detectable signal and a nucleotide sequence complementary to the capture sequence of the RNA reagent of the first component (see col. 4, line 44-45, col. 5, line 7-12, line 23-46), at a first temperature to induce hybridization and thereby to form a pre-hybridized RNA-capture reagent complex (reporter-analyte complex (see col. 5, line 34-46); (b) contacting pre-hybridized RNA-Capture complex with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 4, line 44-46); (d) incubating said mixture at a second temperature to induce hybridization between pre-hybridized RNA-capture reagent complex and the probe on the array, and detecting the he hybridization pattern (col. 4, line 46-49, col. 7, line 27-58).

With regard to claims 17, 22, 36, Dellinger et al. teach said method further comprises passing a base solution to separate the hybridized sequences from the unhybridized probe sequences or a wash step (see col. 6, line 17-27, col. 9, line 43-45, col. 10, line 51-60);

With regard to claim 7-8, 25-26, 50-51 Dellinger et al. teach that the capture sequence is a single-stranded oligonucleotide consisting of at least one adenine base or at least one thymine base (polyA tail or dT tail) (see col. col. 5, line 23-67, col. 6, line 1, line 49-67, col. 7, line 1-4);

With regard to claim 19, Dellinger et al. teach a method for determining the presence of a specific sequence in a RNA reagent of a target sample, said method comprising (a) contacting a first component including an RNA reagent extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7) with a microarray having a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 6, line 17-21); (b) incubating the RNA reagent and the complementary probe nucleic acid sequences on a microarray at a first temperature to hybridize the target nucleotide sequence of the RNA reagent to the complementary probe on the microarray (to form a capture probe-analyte hybrid, see col. 6, line 17-21); (c) contacting a second component comprising a capture reagent comprising a label and a nucleotide complementary to the capture sequence of the RNA reagent of the first component and (d) incubating at a second temperature to induce hybridization between the first and second component , wherein the hybridization signal is detected (see col. 6, line 21-27).

With regard to claim 21, 46, Dellinger et al. teach a method for determining the presence of a specific sequence in a RNA reagent of a target sample, said method comprising (a) contacting a first component including an RNA reagent extracted from a target sample, said RNA reagent having a target nucleic acid sequence and a capture sequence (homopolymeric tail) (see col. 4, line 41-43, col. 5, line 4-7) with a microarray having a plurality of features each comprising a particular probe nucleotide sequence (immobilized capture probe) (see col. 6, line

17-21); (b) incubating the RNA reagent and the complementary probe nucleic acid sequences on a microarray at a first temperature to hybridize the target nucleotide sequence of the RNA reagent to the complementary probe on the microarray (to form a capture probe-analyte hybrid, see col. 6, line 17-21); (c) contacting a second component comprising a capture reagent comprising a label and a nucleotide complementary to the capture sequence of the RNA reagent of the first component and (d) incubating at a second temperature to induce hybridization between the first and second component , wherein the hybridization signal is detected (see col. 6, line 21-27).

With regard to claims 39- 42, Dellinger et al. teach that said probe nucleotide is an oligonucleotide (oligonucleotide sequence, which includes RNA and DNA sequences) (see col. 3, line 6-31);

With regard to claim 43, 45, Dellinger et al. teach that the second component comprises a capture reagent having at least one arm comprising said label and at least one second arm comprising said nucleotide sequence complementary to said capture sequence of the RNA reagent (see col. 8, line 64-67, col. 9, line 1-19, indicates hairpin structures comprise two arms one having a label and other having complementary sequence with a target analyte).

With regard to claim 46, 48, Dellinger et al. teach that the second component comprises a capture reagent having at least one arm comprising said label and at least one second arm comprising said nucleotide sequence complementary to said capture sequence of the RNA reagent (see col. 8, line 64-67, col. 9, line 1-19, indicates hairpin structures comprise two arms one having a label and other having complementary sequence with a target analyte).

With regard to claim 52, Dellinger et al. teach a kit composition comprising (a and b) an array of probe sequences and RNA reagent comprising capture sequence (homopolymeric regions (see col. 2, line 27-32), immobilized capture probe sequences on a solid surface is considered as a microarray); (c) a second component (reporter probe) comprising a complementary nucleotide sequence to said capture sequence on the RNA reagent (analyte homoplymeric region) and said second component further comprises a label (see col. 2, line 30-32, col. 3, line 32-37).

With regard to claim 53, Dellinger et al. teach a kit composition comprising (a and b) an array of probe sequences and RNA reagent comprising capture sequence (homopolymeric regions (see col. 2, line 27-32), immobilized capture probe sequences on a solid surface is considered as a microarray); (c) a second component (reporter probe) comprising a complementary nucleotide sequence to said capture sequence on the RNA reagent (analyte homoplymeric region) and said second component further comprises a label (see col. 2, line 30-32, col. 3, line 32-37).

With regard to claim 54, Dellinger et al. also each that the second component (reporter probe) comprises molecules selected from the group of carbohydrates, proteins and nucleic acids (see col.8, line 60-63);

With regard to claims 55-56, Dellinger et al. teach said capture sequence (homopolymeric region) comprises poly A tail (see col. 5, line 49-67, col. 6, line 15).

However, Dellinger et al. did not teach use of a second component comprising capture reagent with multiple first arms and multiple second arms.

Barberá-Guillem et al. teach a method for detecting a specific nucleic acid in a target sample using a molecular probe having a capture reagent comprising a plurality of first arms (primary dots with plurality of polynucleotide strands) and a plurality of second arms (secondary dots with plurality of polynucleotide strands), wherein the second arms are complementary to the capture sequence of the first component forming a dendrimer of multiple layer , thereby resulting a detectable signal and an exponential increase in the amount of detectable signal that can be detected from a single molecular probe (see col. 2, line 13-46).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. with a molecular probe comprising multiple first and second arms as taught by Barbera-Guillem et al. to achieve expected advantage of amplifying the detectable signal from a single molecular probe in detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. with the step of adding a molecular probe comprising multiple first and second arms as taught by Barbera-Guillem et al. for the purpose of amplifying the detectable signal and increasing the specificity and sensitivity of detecting a target nucleic acid. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in reducing non-specific binding and reduce background noise and enhance specific hybridization signal because Barbera-Guillem et al. explicitly taught that the use of a molecular probe having a capture reagent comprising a plurality of first arms (primary dots with plurality of polynucleotide strands) and a plurality of second arms (secondary dots with plurality of polynucleotide strands), wherein the second arms are complementary to the capture sequence of the first component

forming a dendrimer of multiple layer , thereby resulting a detectable signal and an exponential increase in the amount of detectable signal that can be detected from a single molecular probe (see col. 2, line 13-46).Such modification is considered as obvious over the cited prior art in the absence of secondary considerations.

B. Claims 18, 35, 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-56 above, and further in view of Weston et al (WO99/37805, 29 July 1999).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 3A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach use of blocker probes comprising locked nucleic acid nucleotide (LNA).

Weston et al. teach a method of claims 18, 35, detecting a nucleotide sequence of interest comprising a target DNA and a "blocking oligonucleotide" that hybridizes to the sequence of interest to inhibit re-annealing of the target strand to its complementary strand (see page 11, paragraph 1).

With regard to claim 37-38, Weston et al. teach the blocking oligonucleotide comprises LNA, PNA, DNA or combination thereof. (see page 11, paragraph 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a blocker probe comprising LNA probe as taught by Weston et al. to achieve expected advantage of

developing an enhanced sensitivity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of adding blocker probe as taught by Weston et al. for the purpose of reducing the background noise increasing the specificity and sensitivity of detecting a target nucleic acid. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in reducing non-specific binding and reduce background noise and enhance specific hybridization signal because Weston et al. taught that the use of blocker probe in hybridization assays allow specific and efficient hybridization and minimizes the reannealing of the target strand to its complementary strand thereby reduces non-specific (back-ground noise) hybridization (page 11, line 9-13 of paragraph 1). Such modification is considered as obvious over the cited prior art in the absence of secondary considerations.

C. Claims 4-6, 9-16, 23-24, 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellinger et al. (USPN. 5, 853,993) in view of Barbera-Guillem et al. (US 6,261,779) as applied to claims 1-3, 7-8, 17, 19-21, 22, 25-26, 36, 39-56 above, and further in view of Van Ness et al. (USPN. 6,361,940).

Dellinger et al. in view of Barbera-Guillem et al. teach a method for determining the presence of a specific nucleotide sequence as discussed above in section 3A.

However, neither Dellinger et al. nor Barbera-Guillem et al. teach hybridization temperatures ranging from 50-60^0 C, incubation time, and base solution to separate and purge the hybridized RNA reagent.

Van Ness et al. teach a method for enhancing hybridization and probing or priming specificity, wherein Van Ness et al. teach parameters of a thermal melting profiles (helical coil transition) of an oligonucleotide in hybridization solutions (hybotropic or salt solutions used for separating and purging of hybridized complexes from an array) and the dependency of temperatures (discrimination temperatures) based on the base composition and G-C content of the oligonucleotide probes ranging from 0- 80^0 C (see col. 34, line 48-67, col. 35, line 1-45, col. 45, line 4-33). With regard to claims 4, 6, 22, 24, Van Ness et al. also teach the base solution is sodium hydroxide (see col. 66, line 10-14); With regard to claims 13, 15, 29, 31, Van Ness et al. teach that the probe nucleotide sequences on microarray comprise oligonucleotides and cDNA sequences (see col. 66, line 21-40).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for determining the presence of a specific nucleotide sequence as taught by Dellinger et al. in view of Barbera-Guillem et al. with a the parameters that enhance hybridization specificity such as incubation temperatures and hybridization solutions as taught by Van Ness et al. to achieve expected advantage of developing an enhanced sensitivity and specificity of detecting a target nucleic acid. An ordinary practitioner would have been motivated to combine the method of Dellinger et al. in view of Barbera-Guillem et al. with the step of adding said hybridization parameters as taught by Van Ness et al. for the purpose of increasing the specificity of hybridization assay. An ordinary person skilled in the art would have a reasonable expectation of success that such modification would result in enhance specificity of hybridization signal because Van Ness et al. explicitly taught that the parameters to optimize hybridization conditions and to increase hybridization

specificity (col. 56, line 52-67, col. 57, line 1-16). Such modification is considered as obvious over the cited prior art in the absence of secondary considerations. Further, selection of specific hybridization conditions including incubation time, temperatures, oligonucleotide probes represents routine optimization with regard to sequence, length and composition of the oligonucleotide, which routine optimization parameters are explicitly recognized in Van Ness et al. As noted in *In re Aller*, 105 USPQ 233 at 235,More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the selection of hybridization conditions performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Response to arguments:

4. With regard to the rejection of claims 17, 53-56 under 35 USC 112, second paragraph, Applicants' amendment and arguments are fully considered and found persuasive and the rejection is withdrawn in view of the amendment.

5. With regard to the rejection of claims 1-55 under obviousness-type double patenting, Applicants' amendment and arguments are fully considered Applicants request clarification of the pub No. for Application 10/825,766. It is noted that Examiner inadvertently made a typo error. The correct Pub No. is 2005/0202449 for application 10/825,776. The rejections are maintained herein since the scope of the co-pending claims remain within the scope of the instant

claims and until Applicants provide complete response to the rejections in view of the above clarification.

6. With regard to the provisional rejection under 35 USC 102 (e), Applicants' arguments are fully considered and found persuasive and the rejections are withdrawn in view of the arguments.

7. With regard to the rejection under 35 USC 102(b) as being anticipated by Dellinger et al., Applicants' amendment and arguments are fully considered and found persuasive and the rejection is withdrawn in view of the amendment and new grounds of rejections.

8. With regard to the rejection under 35 USC 103(a), Applicants' amendment and arguments are fully considered and found persuasive and the rejection is withdrawn in view of the amendment and new grounds of rejections.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637.

Prabha Chunduru
SURYAPRABHA CHUNDURU 8/2/06
PATENT EXAMINER